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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/875,349	06/05/2001	John C. Hiserodt	IRVN001DIV	8040

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EXAMINER

YAEN, CHRISTOPHER H

ART UNIT	PAPER NUMBER
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1642

DATE MAILED: 06/03/2003

9

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/875,349

Applicant(s)

HISERODT ET AL.

Examiner

Christopher H Yaen

Art Unit

1642

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 11 March 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 31-50 and 52-81 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 31-50 and 52-81 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

1. The amendment filed 3/11/2003 (paper no. 8) is acknowledged and entered into the record. Accordingly, claim 51 is canceled, claims 63-81 are newly added.
2. Therefore, claims 31-50 and 52-81 are depending and examined on the merits.

Claim Rejections Withdrawn - 35 USC § 112, 2nd paragraph

3. The rejection of claims 31-62 under 35 USC 112, 2nd paragraph is withdrawn in view of the arguments and amendments.

Claim Rejections Withdrawn - 35 USC § 102

4. The rejection of claims 31-33,36,38,40,49,52,57, and 59-62 under 35 USC 102(a) as being anticipated by Kimura *et al* is withdrawn in view of the arguments presented by the applicant.

Claim Rejection Maintained - 35 USC § 112, 1st paragraph

5. The rejection of claims 31-60 and now newly added claims 61-78 under 35 USC 112, 1st paragraph is maintained for the reasons of record. Applicant argues that the construction of a cell that expresses a membrane-associated cytokine is spelled out and is easily accomplished from the disclosure of the instant application and from a reference filed post filing of the instant application. However, applicant's arguments are not on point to the arguments presented by the examiner. The Office Action mailed 10/3/2002 raised issues of unpredictability in the field. The applicant has not addressed the issues concerning the effects of fusing a cytokine to a membrane and has only addressed the "making aspects" of the rejection. The response filed 3/11/2003 has not specifically address the "using" aspects of the invention so that one of skill in the art can

be enabled to "use" the instant invention. The fusion of two different proteins and the coupling of a protein to a cell surface is a well established technique in the art, but the use of a cancer cell expressing a recombinant cytokine fused to its surface has not been taught. Furthermore, the specification has only taught one specific example of a membrane associated cytokine, which as is taught in the art, a cytokine that naturally occurs in either secreted or membrane forms.

Claim Rejections Maintained - 35 USC § 102

6. The rejection of claims 31-33, 35-37, 40, 49, 52, and, 54-62, and now newly added claims 67-70, 72, 74, and 78-79 under 35 USC 102(a) as being anticipated by *Jadus et al* is maintained for the reasons of record. Applicant argues that the inventors of the instant application and the authors of the prior art reference were collaborator and therefore the reference cited does not qualify as a 102(a) reference. Applicant also argues that the nature of the invention and that disclosed by *Jadus et al* are different. Applicant's arguments are not found persuasive. The legal standard for using a reference as a prior art reference under 35 USC 102(a) is that the reference must be disclosed by "another," before the earliest priority date claimed by the instant application. Regardless of the working relationship established between the inventors of the instant invention and the authors of the prior art reference, the reference cited is by "another" and before the priority date established by the applicant, thereby validating the reference as a legitimate 102(a) reference. With regards to the content of the disclosed reference, *Judas et al* clearly discloses the use of a cell line that has been recombinantly modified to express the membrane bound form of M-CSF, called mM-

CSF. Although the cell line used, namely the T9 cells, were indeed used only for in vitro studies, there was another cell line the NBXFO that are cancer derived that could be used for administration. Furthermore, Jadus *et al* contemplates that therapeutic approaches using mM-CSF in transfected tumor cells could provide for a useful method of stimulating a system immune response to cancers.

Claim Rejections Maintained - 35 USC § 102

7. The rejection of claims 31-32,52,55,57,61 and now newly added claims 67-69 under 35 USC 102(a) as being anticipated by Tuck *et al* is maintained for the reasons of record. Applicant argues that Tuck *et al* does not suggest the use of the cells as a pharmaceutical composition and only uses the cells for in vitro experimentation. Applicant's arguments have been carefully considered but are not found persuasive because the product and method of developing the product are the same. As it pertains to the product claims, the product taught by Tuck *et al* is identical to that taught by the instant application and regardless of the its intended use, the product is still the product. The intended use of a product does not carry any patentable weight, as such the addition of pharmaceutical excipients to a product is an intended use of the same product.

New Arguments

Claim Rejections - 35 USC § 112

8. Claims 31-50 and 52-81 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

9. With regard to claims reciting of the term "inactivated", it is unclear as to the intended meaning of this term. Does the applicant intend for the cell to be dead, or does the applicant intend for the cell to be a ghost cell which is essentially used for its structural features?

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

11. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 31-33, 35-37, 40, 49, 52, 54-62, 67-70, 72, 74, and 78-79 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jadus *et al* (Blood 1996 June;87(12):5232-5241). Claims are drawn to a pharmaceutical composition comprising a cell recombinantly expressing a cytokine, M-CSF, associated with the

Art Unit: 1642

outer membrane wherein the cell is inactivated and also expresses TAAs. The claims are also drawn to a method of producing the said cell.

Jadus *et al* discusses the role of macrophage activation when in the presence of cells expressing a membrane bound form of M-CSF. Jadus *et al* further teaches the use of a cancer cell line, which presumably in the absence of evidence to the contrary would also have on its surface TAAs. And lastly, Jadus *et al* specifically states that the use of tumor cells expressing membrane bound forms of M-CSF would be killed by macrophages and then subsequently be turned into antigen presenting cells that would allow the stimulation of an immune response.

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to make a tumor cell expressing on its surface a membrane bound cytokine and a tumor associated antigen because Jadus *et al* has taught all the elements of the invention. One would have been motivated because Jadus *et al* has already taught the construction of a cell that has on its surface both a membrane bound cytokine, mM-CSF, and a TAA. Jadus *et al* then points the applicant in the direction of the instant invention wherein Jadus *et al* states that tumor cell lines that express mM-CSF would be able to reduce tumor burden because first macrophages would attack the tumor and then the tumor cell line itself would become the antigen presenting cell wherein a systemic immune response to the cancer would be established (see page 5239 1st column). One of skill would have expected a reasonable amount of success in the making a cell because the in vitro data generated

by Jadus *et al* substantiates the role mCSF transfected cells have in generating an anti-tumor response.

Conclusion

12. No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher H Yaen whose telephone number is 703-305-3586. The examiner can normally be reached on Monday-Friday 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-

Application/Control Number: 09/875,349


Page 8

Art Unit: 1642

308-4242 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Christopher Yaen
Art Unit 1642
June 2, 2003


ANTHONY C. CAPUTA
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600